

DOCKET NO: 282726US8X

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :  
OLIVER HARNACK, ET AL. : EXAMINER: YU, MELANIE J.  
SERIAL NO: 10/631,351 :  
FILED: JULY 31, 2003 : GROUP ART UNIT: 1641  
FOR: METHOD OF ATTACHING :  
HYDROPHILIC SPECIES TO  
HYDROPHILIC MACROMOLECULES  
AND IMMOBILIZING THE  
HYDROPHILIC MACROMOLECULES  
ON A HYDROPHOBIC SURFACE

APPEAL BRIEF

COMMISSIONER FOR PATENTS  
ALEXANDRIA, VIRGINIA 22313

SIR:

Further to the February 8, 2008 Notice of Appeal, this is an Appeal from the August 8, 2007 Final Rejection.

**I. REAL PARTY IN INTEREST**

The real party in interest in this appeal is Sony Deutschland GmbH, Berlin, Germany.

**II. RELATED APPEALS AND INTERFERENCES**

Appellants, Appellants' legal representative and the assignee are aware of no appeals, interferences, or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

**III. STATUS OF CLAIMS**

Claims 2-20 are pending and stand rejected.

Claims 1 and 21-23 have been cancelled.

The rejections of claims 2-20 are being appealed.

**IV. STATUS OF AMENDMENTS**

No Amendment After Final Rejection has been filed.

**V. SUMMARY OF CLAIMED SUBJECT MATTER**

Independent claim 2 is directed to a method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface by first providing a hydrophobic surface, then changing the nature of that hydrophobic surface by immobilizing hydrophilic macromolecules on the hydrophobic surface, and finally exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the

hydrophilic species are attached to the hydrophilic macromolecules. *See, e.g.*, specification page 3, lines 1-8 and claim 2. Claims 3-20 depend directly or indirectly from claim 2.

## **VI. GROUND OF REJECTION TO BE REVIEWED ON APPEAL**

### **A. Ford and Klein**

Claims 2-11, 14-18 and 20 are rejected under 35 U.S.C. §103(a) over U.S. Patent Application Publication No. 2002/0065242 to Ford et al. ("Ford") in view of Klein et al., "Ordered stretching of single molecules of deoxyribose nucleic acid between microfabricated polystyrene lines," Applied Physics, 78:2396-2398 (2001) ("Klein").

### **B. Ford, Klein and Tajima**

Claims 12 and 13 are rejected under 35 U.S.C. §103(a) over Ford in view of Klein and U.S. Patent No. 4,649,071 to Tajima et al. ("Tajima").

### **C. Ford, Klein and Berning**

Claim 19 is rejected under 35 U.S.C. §103(a) over Ford in view of Klein and Berning et al., "<sup>198</sup>Au Labeled Hydroxymethyl Phosphines as Models for Potential Therapeutic Pharmaceuticals," Nuclear Medicine and Biology, 25: 577-583 (1998) ("Berning").

### **D. Ford and Schueller**

Claims 2, 3 and 14-18 are rejected under 35 U.S.C. §103(a) over Ford in view of U.S. Patent Application Publication No. US 2002/0050220 to Schueller et al. ("Schueller").

**E. Ford, Schueller and Tajima**

Claims 12 and 13 are rejected under 35 U.S.C. §103(a) over Ford in view of Schueller and Tajima.

**F. Ford, Schueller and Berning**

Claim 19 is rejected under 35 U.S.C. §103(a) over Ford in view of Schueller and Berning.

**G. 049 Application and Caldwell**

Claims 2-6, 11, 15 and 17-19 is rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4, 14-16 and 20 of U.S. Patent Application No. 09/990,049 (the "049 application") in view of U.S. Patent No. 5,516,703 to Caldwell et al. ("Caldwell"). Appellants have requested that the double patenting rejection over the 049 application and Caldwell be held in abeyance until the 049 application issues as a patent or the present application has been otherwise indicated to be in condition for allowance. Accordingly, the rejection over the 049 application and Caldwell is not addressed in this appeal.

**VII. ARGUMENT**

Appellants submit that the outstanding rejections should be reversed for the following reasons.

**A. Ford and Klein**

As indicated above, claims 2-11, 14-18 and 20 are rejected under 35 U.S.C. §103(a) over Ford in view of Klein.

Claim 2 recites "[a] method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, said method comprising the steps: (i) providing a hydrophobic surface, (ii) immobilizing hydrophilic macromolecules on the hydrophobic surface, (iii) exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules" (emphasis added). Ford and Klein do not disclose or suggest such a method.

The Examiner relies on Ford for its alleged disclosure of providing a hydrophilic substrate, immobilizing hydrophilic nucleic acids on the substrate, and metallizing the immobilized nucleic acids with a hydrophilic species. *See* December 19, 2006 Office Action, pages 2 to 3. The Examiner relies on Klein for its alleged disclosure of immobilizing a hydrophilic nucleic acid on a hydrophobic substrate. *See* December 19, 2006 Office Action, page 3. It is undisputed that neither Ford nor Klein discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species.

The Examiner asserts that it would have been obvious to combine the teachings of Ford and Klein to obtain a method "that is easy to employ and results in high yield." *See* December 19, 2006 Office Action, page 3. As is well-settled, a *prima facie* case of obviousness based on a proposed combination of references (e.g., replacing the hydrophilic

substrate of Ford with the hydrophobic substrate of Klein) will only stand if one of ordinary skill would have had a reasonable expectation of success upon making the modification. *See, e.g.*, MPEP §2143.02 (citing *In re Merck & Co., Inc.*, 800 F.2d 1091 (Fed. Cir. 1986)). One of ordinary skill in the art would have had no reason to expect that the method of Ford would function employing a hydrophobic substrate as disclosed in Klein.

It is well known that hydrophilic species (e.g., water soluble globular proteins or antibodies), notwithstanding their hydrophilicity, adsorb irreversibly to hydrophobic surfaces upon contact. This property creates difficulties for those of ordinary skill in the art, for example, when performing protein purification in the presence of plastic lab ware. When an aqueous protein solution contacts hydrophobic surfaces, such as plastic test tubes or dialysis tubing, protein material is irreversibly lost. This phenomenon of non-specific adsorption is described, for example, in Caldwell (cited by the Examiner in the outstanding obviousness-type double patenting rejection). *See, e.g.*, Caldwell, column 1, lines 44 to 59. One of ordinary skill in the art would not expect to be able to control the deposit of hydrophilic species on a hydrophobic substrate. Rather, one of ordinary skill in the art would expect that the hydrophilic species would bind randomly to the hydrophobic substrate.

When the foregoing phenomenon was brought to the Examiner's attention, the Examiner asserted that Caldwell does not demonstrate non-specific adsorption, as discussed above. *See* August 8, 2007 Office Action, page 9. Rather, the Examiner asserted that Caldwell's teachings are limited to the non-specific adsorption of antibodies to hydrophobic substrates and, thus, would not discourage a skilled artisan from attempting to employ the hydrophilic species of Ford (gold nanoparticles) with a hydrophobic substrate. *See* August 8, 2007 Office Action, page 9. While Appellants do not agree with the Examiner's

characterization of Caldwell, Appellants provided the Examiner with a further reference demonstrating that one of ordinary skill in the art would expect hydrophilic gold nanoparticles to adsorb non-specifically to a hydrophobic substrate. *See* Fan, H., et al., "Adsorption of Surface-Modified Colloidal Gold Particles onto Self-Assembled Monolayers: A Model System for the Study of Interactions of Colloidal Particles and Organic Surfaces," *Langmuir* 1997, 13, 119-121 ("Fan") (copy attached hereto in Evidence Appendix).

Fan describes the adsorption of gold nanoparticles to self-assembled monolayers. In particular, Fan describes the manner in which hydrophilic gold nanoparticles adsorb to surfaces having differing degrees of hydrophobicity. As can be seen, for example, from FIG. 3 of Fan, the more hydrophobic a surface is, the greater the adsorption of gold particles. As stated in Fan, "results confirm that the colloids studied adsorb from the aqueous solution more extensively to hydrophobic surfaces." *See* Fan, Abstract. Moreover, "adsorption of colloidal gold particles onto SAMs indicate that adsorption of colloidal particles onto organic surfaces from aqueous suspensions follows thermodynamic predictions to a considerable extent: more colloidal particles adsorb to more hydrophobic organic surfaces." *See* Fan, page 121 (emphasis added). Thus, as discussed above with respect to Caldwell, one of ordinary skill in the art would not expect to be able to control the deposit of hydrophilic species on a hydrophobic substrate and, thus, one of ordinary skill in the art would not expect success upon combining Ford and Klein as proposed by the Examiner.

In view of the foregoing, one of ordinary skill in the art would not expect success if attempting to expose hydrophilic macromolecules immobilized on a hydrophobic substrate to a hydrophilic species, such as metal nanoparticles, to bind the hydrophilic species to the hydrophilic macromolecules. Rather, one of ordinary skill in the art would expect non-

specific reactions between the hydrophilic species and both the hydrophobic substrate and the hydrophilic macromolecules. This non-specific reactivity would have dissuaded one of ordinary skill in the art from attempting to replace the hydrophilic substrate of Ford with the hydrophobic substrate of Klein.

In addition, Appellants note that Klein, taken either as a whole or in view of its specific teachings does not fairly suggest employing hydrophobic substrates in broader contexts, as proposed by the Examiner. See August 8, 2007 Office Action, page 10. For example, Klein discloses that "patterned DNA on a substrate can serve as templates for wires and for two and three-dimensional nanoscale devices." See Klein, page 2396, left-hand column, lines 25 to 27. However, this teaching is plainly in the context of hydrophilic substrates, such a glass or silane-treated substrates. See Klein, page 2396, left-hand column, lines 14 to 18. In view of this teaching, one of ordinary skill in the art would understand that hydrophilic substrates could potentially serve as templates for wires, etc. However, hydrophobic substrates would remain, even in the view of a skilled artisan versed with the teachings of Klein, plagued by the non-specific adsorption issues discussed above.

Appellants surprisingly discovered that exposure of a hydrophilic species (e.g., an aqueous solution of gold nanoparticles) to a hydrophobic substrate (e.g., polystyrene) on which hydrophilic macromolecules are immobilized provides a desirable result. Namely, the hydrophilic species binds specifically (i.e., almost exclusively) to the hydrophilic molecule, and not the hydrophobic substrate. See, e.g., present specification, pages 10 to 11. That is, the hydrophilic species does not bind non-specifically to the hydrophobic substrate as would have been expected in view of past experience relating to the binding of hydrophilic species to hydrophobic substrates.



As neither Ford nor Klein discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species, and one of ordinary skill in the art would not expected success upon combining Ford and Klein as proposed by the Examiner, the combination of Ford and Klein would not have rendered obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford and Klein. Claims 3-11, 14-18 and 20 depend from claim 2 and, thus, also would not have been rendered obvious by Ford and Klein. Accordingly, reversal of the rejection is respectfully requested.

**B. Ford, Klein and Tajima**

As indicated above, claims 12 and 13 are rejected under 35 U.S.C. §103(a) over Ford in view of Klein and Tajima.

Claim 2 is set forth above. For the reasons discussed above, Ford and Klein do not disclose or suggest the method of claim 2. Tajima does not remedy the deficiencies of Ford and Klein. Tajima is cited for its alleged disclosure of the water contact angle of polystyrene. See August 8, 2007 Office Action, page 4. However, Tajima, like Ford and Klein fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Klein and Tajima fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Klein and Tajima. Claims 12 and 13 depend from claim 2 and, thus, also would not have been rendered obvious by Ford, Klein and Tajima. Accordingly, reversal of the rejection is respectfully requested.

**C. Ford, Klein and Berning**

As indicated above, claim 19 is rejected under 35 U.S.C. §103(a) over Ford in view of Klein and Berning.

Claim 2 is set forth above. For the reasons discussed above, Ford and Klein do not disclose or suggest the method of claim 2. Berning does not remedy the deficiencies of Ford and Klein. Berning is cited for its alleged disclosure of tris(hydroxymethyl)phosphine-gold nanoparticles. *See* August 8, 2007 Office Action, page 4. However, Berning, like Ford and Klein fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Klein and Berning fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Klein and Berning. Claim 19 depends from claim 2 and, thus, also would not have been rendered obvious by Ford, Klein and Berning. Accordingly, reversal of the rejection is respectfully requested.

**D. Ford and Schueller**

As indicated above, claims 2, 3 and 14-18 are rejected under 35 U.S.C. §103(a) over Ford in view of Schueller.

Claim 2 is set forth above. Ford and Schueller fail to disclose or suggest such a method.

The Examiner relies on Ford for its alleged disclosure of providing a hydrophilic substrate, immobilizing hydrophilic nucleic acids on the substrate, and metallizing the immobilized nucleic acids with a hydrophilic species. *See* August 8, 2007 Office Action, page 5. The Examiner relies on Shueller for its alleged disclosure of immobilizing a hydrophilic nucleic acid on a hydrophobic substrate. *See* August 8, 2007 Office Action, page 5. It is undisputed that neither Ford nor Schueller discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Appellants submit that one of ordinary skill in the art would not have expected that the method of Ford would function employing a hydrophobic substrate as disclosed in Schueller, for the reasons discussed above with respect to Ford and Klein.

As neither Ford nor Schueller discloses or suggests the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species, and one of ordinary skill in the art would not have expected success upon combining Ford and Schueller as proposed by the Examiner, the combination of Ford and Schueller would not have rendered obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford and Schueller. Claims 3 and 14-18 depend from claim 2 and, thus, also would not have been rendered obvious by Ford and Schueller. Accordingly, reversal of the rejection is respectfully requested.

**E. Ford, Schueller and Tajima**

As indicated above, claims 12 and 13 are rejected under 35 U.S.C. §103(a) over Ford in view of Schueller and Tajima.

Claim 2 is set forth above. For the reasons discussed above, Ford and Schueller do not disclose or suggest the method of claim 2. Tajima does not remedy the deficiencies of Ford and Schueller. Tajima is cited for its alleged disclosure of the water contact angle of polystyrene. *See* August 8, 2007 Office Action, page 6. However, Tajima, like Ford and Schueller fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Schueller and Tajima fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Schueller and Tajima. Claims 12 and 13 depend from claim 2 and, thus, also would not have been rendered obvious by Ford, Schueller and Tajima. Accordingly, reversal of the rejection is respectfully requested.

**F. Ford, Schueller and Berning**

As indicated above, claim 19 is rejected under 35 U.S.C. §103(a) over Ford in view of Schueller and Berning.

Claim 2 is set forth above. For the reasons discussed above, Ford and Schueller do not disclose or suggest the method of claim 2. Berning does not remedy the deficiencies of Ford and Schueller. Berning is cited for its alleged disclosure of tris(hydroxymethyl) phosphine-gold nanoparticles. *See* August 8, 2007 Office Action, page 7. However,

Berning, like Ford and Schueller fails to disclose or suggest the combination of immobilizing hydrophilic macromolecules on a hydrophobic surface and exposing the macromolecules to a hydrophilic species. Accordingly, the combination of Ford, Schueller and Berning fails to render obvious claim 2.

As explained, claim 2 would not have been rendered obvious by Ford, Schueller and Berning. Claim 19 depends from claim 2 and, thus, also would not have been rendered obvious by Ford, Schueller and Berning. Accordingly, reversal of the rejection is respectfully requested.

**G. 049 Application and Caldwell**

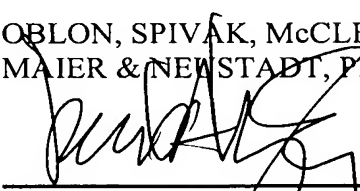
Claims 2-6, 11, 15 and 17-19 is rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4, 14-16 and 20 of the 049 application in view of Caldwell. As discussed above, Appellants have requested that the double patenting rejection over the 049 application and Caldwell be held in abeyance until the 049 application issues as a patent or the present application has been otherwise indicated to be in condition for allowance. Accordingly, the rejection over the 049 application and Caldwell is not addressed in this appeal.

**VIII. CONCLUSION**

For the above reasons, it is respectfully requested that all outstanding rejections of the pending claims be REVERSED.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
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## **CLAIMS APPENDIX**

Claim 1 (Cancelled).

Claim 2 (Previously Presented): A method of attaching hydrophilic species to hydrophilic macromolecules immobilized on a hydrophobic surface, said method comprising the steps:

- (i) providing a hydrophobic surface,
- (ii) immobilizing hydrophilic macromolecules on the hydrophobic surface,
- (iii) exposing the hydrophilic macromolecules immobilized on the hydrophobic surface to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules.

Claim 3 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species comprises nanoparticles.

Claim 4 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species is in solution.

Claim 5 (Previously Presented): A method according to claim 2, comprising the additional step:

- (iv) growing the attached hydrophilic species to a larger size.

Claim 6 (Previously Presented): A method according to claim 5, characterized in that growing the attached hydrophilic species to a larger size is achieved by exposing the attached hydrophilic species to an electroless plating solution.

Claim 7 (Previously Presented): A method according to claim 2, characterized in that immobilizing the hydrophilic macromolecules on the hydrophobic surface occurs by applying the hydrophilic macromolecules to the hydrophobic surface.

Claim 8 (Previously Presented): A method according to claim 7, characterized in that applying the hydrophilic macromolecules to the hydrophobic surface occurs by a process selected from spin-coating, dip-coating, drop-casting, stamping, molecular combing, spraying-techniques, inkjet-printing and doctor-blading.

Claim 9 (Previously Presented): A method according to claim 2, characterized in that exposing the hydrophilic macromolecules to hydrophilic species, whereby the hydrophilic species are attached to the hydrophilic macromolecules, occurs over a period of time between 1 second and 120 minutes.

Claim 10 (Previously Presented): A method according to claim 9, characterized in that exposing the hydrophilic macromolecules to hydrophilic species occurs over a period of time between 10 seconds and 10 minutes.

Claim 11 (Previously Presented): A method according to claim 4, characterized in that the solution is a solution of the hydrophilic species in water or of the hydrophilic species in a water-miscible organic solvent/water mixture.

Claim 12 (Previously Presented): A method according to claim 2, characterized in that water has a contact angle on the hydrophobic surface in the range of from 30° to 110°.



Claim 13 (Previously Presented): A method according to claim 12, characterized in that water has a contact angle on the hydrophobic surface in the range of from 60° to 110°.

Claim 14 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species is selected from the group comprising water soluble metal nanoparticles,

semiconductor nanoparticles and dielectric (insulator) nanoparticles, hydrophilic clusters and metallic complexes.

Claim 15 (Previously Presented): A method according to claim 3, characterized in that the nanoparticle has a core and comprises a metal or metal oxide in the core, where the metal is selected from the group comprising Fe, Co, Ni, Cu, Ru, Rh, Pd, Os, Ir, Ag, Pt, Au or combinations, especially alloys of these metals.

Claim 16 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic macromolecules are selected from the group comprising nucleic acids, proteins, dendrimers, latex spheres, polyelectrolytes, and water-soluble polymers.

Claim 17 (Previously Presented): A method according to claim 16, characterized in that the nucleic acid is selected from the group comprising DNA, RNA, PNA, CNA, oligonucleotides, oligonucleotides of RNA, A-DNA, B-DNA, Z-DNA, polynucleotides of DNA, polynucleotides of RNA, T-junctions of nucleic acids, triplexes of nucleic acid, quadruplexes of nucleic acids, domains of non-nucleic acid polymer-nucleic acid block-copolymers and combinations thereof.

Claim 18 (Previously Presented): A method according to claim 17, characterized in that the nucleic acid is double-stranded or single-stranded.

Claim 19 (Previously Presented): A method according to claim 2, characterized in that the hydrophilic species is selected from the group comprising tris(hydroxymethyl)phosphine-gold nanoparticles (THPAuNPs).

Claim 20 (Previously Presented): A method according to claim 6, characterized in that the electroless plating solution comprises a gold salt and a reducing agent.

Claims 21-23 (Cancelled).

**EVIDENCE APPENDIX**

Fan, H., et al., "Adsorption of Surface-Modified Colloidal Gold Particles onto Self-Assembled Monolayers: A Model System for the Study of Interactions of Colloidal Particles and Organic Surfaces," *Langmuir* 1997, 13, 119-121 ("Fan"). Fan was submitted as an attachment to the Request for Reconsideration filed on December 10, 2007, and was considered by the Examiner in the January 28, 2008 Advisory Action.

**RELATED PROCEEDINGS APPENDIX**

None.